Vaccines and Influenza
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Mary A. Ullman, PharmD
Department of Experimental and Clinical Pharmacology
McGuire Translational Research Facility Room 4-500
ullma020@umn.edu

Objectives

1) **Compare and contrast live attenuated vaccines and inactivated vaccines**
2) **Identify possible drug interactions with vaccines**
3) **Differentiate between valid and not valid contraindications and/or precautions to use of a given vaccine**
4) **Recommend appropriate vaccines, including number of doses and time periods, for a patient based on age and/or risk factors**
5) **Choose an appropriate therapy for the prevention or treatment of influenza, given a patient case**

- Key terms
  - Immunity
    - Ability of the human body to tolerate the presence of material indigenous to the human body and to eliminate foreign material
  - Passive immunity
    - Gained immunity from products produced by an animal or human and transferred to another human
  - Active immunity
    - Immunity produced by a person's own immune system after exposure to an antigen
  - Antigen
    - Live or inactivated substance capable of producing an immune response
  - Antibody
    - Protein molecules produced by B lymphocytes to help eliminate an antigen

- Types of vaccines
  - Live attenuated vaccines
    - Source
      -
    - Number of doses required
      -
    - Because this type of vaccine contains a live virus, caution must be used in immunocompromised patients
    - Vaccine failure will occur if antibodies to the virus or bacteria are present
  - Inactivated vaccines
    - Source
      -
    - Number of doses required
      -
      -
    - Booster shots are required as antibody concentrations will diminish over time
  - Polysaccharide vaccines
    - Source
      -
    - Polysaccharide chain acts as an antigen, eliciting an immune response
    - Booster shots do not offer an advantage to increasing immunity
  - Recombinant vaccines
    - Source
      -
    - Examples of genetic engineering
      - Removal of the ability to cause disease
      - Reproduction of the organism is limited to a certain cell type
      - Replication and production of antigen
  - Classification of common vaccines

Live attenuated	Inactivated	Polysaccharide	Recombinant
Measles Mumps Rubella Varicella Zoster Rotavirus (PO) Yellow fever Vaccinia Influenza (intranasal) Typhoid (PO)	Polio Hepatitis A Hepatitis B Influenza (IM) Pertussis Diptheria Tetanus HPV Rabies	Pneumococcal Meningococcal *Salmonella* typhi *Haemophilus influenza* type B	Hepatitis B HPV Typhoid (PO) Influenza (intranasal)

- Vaccine Basics
  - Adverse Reactions
    - Three types
      - Local reactions: pain, swelling, redness at injection site
      - Systemic: fever, malaise, headache, anorexia
      - Anaphylactic reactions
    - Special process for reporting adverse reactions through the Vaccine Adverse Event Reporting System (VAERS)
      - Form available at www.vaers.hhs.gov

  - Allergies
    - Both the   and the   are important to obtain from patient (or guardian)
    - If a patient has anaphylaxis to any vaccine or component, contraindication to administer
    - List of common allergies and vaccines ***NOT*** to be given

Allergy	Vaccines contraindicated
Eggs	Influenza vaccine, yellow fever
Gelatin	Varicella, MMR
Neomycin	MMR, inactivated polio vaccine, varicella, vaccinia
Polymyxin B	Inactivated polio vaccine, vaccinia
Latex	All vaccines; Vials containing vaccine to be administered should use a vial without natural rubber

  - Contraindications
    - Valid contraindications
      -
        - Vaccines include intranasal flu, MMR, PPV, rabies, PO typhoid, vaccinia, varicella, yellow fever
        - Contraindication may extend beyond individual dependent on vaccine
          - Household contacts: live flu vaccine, vaccinia
          - Family history: varicella
      -
        - Vaccines include
          - MMR and varicella – pregnancy should be avoided for 4 weeks after immunization
          - Intranasal flu and vaccinia
          - Inactivated polio vaccine and Hepatitis A – may be given to those at high risk
          - Japanese encephalitis – if travelling to endemic country, weigh risk vs benefit
          - Yellow fever – Should try to avoid travel to endemic country until pregnancy complete; weigh risk vs benefit; should obtain waiver for vaccine prior to travel
          - HPV and typhoid – not contraindicated but no data exist on safety

        - Contraindications concerned with diphtheria/tetanus/acellular pertussis (DTaP) vaccine
            - Encephalopathy within 7 days of DTaP (no other cause apparent)
            - Children with neurological disorders should be evaluated as well
            - Several precautions also exist
        - Guillian-Barré Syndrome
            - Intranasal flu
            - Risk vs benefit should be weighed for individuals contemplating IM influenza and DTaP
    - *Invalid* contraindications
        -
        - Preterm birth
        -
        - Breastfeeding (excluding vaccinia)
        - Penicillin allergy
        - Duck or feather allergies
        - Allergies in blood relatives
        -
        -
            - Thimerosal originally identified as causative agent thought to cause autism
            - In July 1999, an agreement was reached that thimerosal should be reduced or eliminated in vaccines as a precautionary measure
            - Additionally, multiple studies have not support a causal link between vaccines (specifically MMR) and autism
            - If still concerned, consult additives and consider using single-use vaccines

- Dosing
    - Number of doses dependent on vaccine tpe
        - Live attenuated vaccine
            - First dose:
            - Second dose:
        - Inactivated vaccine
            -
            - Additional boosters may also be needed, dependent on how long individual is at risk for disease
    - General wisdom about vaccine schedules
        -
        - Vaccination only counts as being valid if given up to 4 days prior to minimum interval or age

- Interactions
    - Immunoglobulin preparations
        - Have no effect on inactivated vaccines
        - Antibody presence decreases immune system response to live attenuated vaccines
        - How to avoid interaction
            - If vaccine given first, wait at least 2 weeks before giving immunoglobulin
            - If immunoglobulin is given first, time period is dependent on vaccine and immunoglobulin, but a three-month interval is at least required
    - Other vaccines
        -
        - Some vaccines may interact if given on separate days
            - Live attenuated vaccines and intranasal flu vaccines should be separated by at least 4 weeks
    - Antibiotics
        - Intranasal flu vaccine
            - Influenza antivirals
        - Varicella
            - Antivirals
        - Oral typhoid
            - Sulfonamides

        - Other antimicrobials
        - Should be separate by at least 24 hours

- Storage and Reconstitution
    - Package insert should be read carefully
        - Refrigerated or frozen?
        - How to reconstitute?
    -
        - Do not store dose in syringes
    - Do not re-freeze frozen vaccines and discard 30 minutes after reconstitution

- Recommended Immunizations
    - Hepatitis B
        - Who?
            -
            - At risk adults
                - Household contacts, sex partners of HBsAg+ persons
                - IVDU
                - Heterosexuals $\geq$ 1 partner/ 6 months
                - MSM
                - Recent STD diagnosis
                - HD and patient with renal disease likely to progress to dialysis
                - Receiving certain blood products
                - Healthcare workers, public safety workers
                - Clients, staff of developmentally disabled institutions
                - Inmates in long-term correctional facilities
                - International travelers
        - When?
            - **Dose 1**: all newborns prior to discharge
                -
            - **Dose 2**: 1 – 2 months (or at least 4 weeks after Dose 1)
            - **Dose 3**: 6 – 18 months (or at least 8 weeks after Dose 2, 16 weeks after Dose 1)
        - If mother is HBsAg+, Dose 1 should be administered within 12 hours of birth in addition to hepatitis B immune globulin
        - No routine need for boosters once complete 3-dose series

    - Rotavirus
        - Who?
            - Infants
            -
            - Caution should be used for
                - Infants with severe acute gastroenteritis
                - Chronic GI disease
                - History of intussusceptions
        - When?
            - Dose 1: 2 months (may be given as early as 6 weeks)
            - Dose 2: 4 months (or at least 4 weeks after Dose 1)
            - Dose 3: 6 months (or at least 4 weeks after Dose 2; no later than 32 weeks)

    - DTaP (Diptheria, Tetanus, acellular Pertussis)
        - Who?
            -
            - Which components are given is dependent on age and previous vaccination history
        - When?
            - DTaP
                - Dose 1: 2 months
                - Dose 2: 4 months (at least 4 weeks after Dose 1)
                - Dose 3: 6 months (at least 4 weeks after Dose 2)
                - Dose 4: 15 – 18 months (at least 6 months after Dose 3)
                - Dose 5: 4 – 6 years

        - Do not give if Dose 4 was received at an age older than 4 years old
    - Td, Tdap
      - Booster Tdap
        - 11 – 12 years if 5 years since DTaP
      - Booster Td

- *Haemophilus influenza* type B (Hib)
  - Who?
      - Functional or anatomic asplenia
      - Immunodeficiency
      - Immunosuppression from cancer chemotherapy, HIV, or hematopoietic stem cell transplant
  - When?
    - Should be at least 6 weeks old before Dose 1
    - Dosing dependent on which commercial vaccine is used
      - ActHib
        - Dose 1: 2 months
        - Dose 2: 4 months
        - Dose 3: 6 months
        - Dose 4: 12 – 15 months
      - PedvaxHIB, Comvax
        - Dose 1: 2 months
        - Dose 2: 4 months
        - Dose 3: 12 – 15 months
    - If child is behind on vaccinations and is aged 15 months to 5 years, only one dose is required
    - Older children and adults at high risk should receive at least one pediatric dose of any Hib conjugate vaccine

- ; Pneumococcal Conjugate vaccine (PCV)
  - Provides protection against the 7 serotypes which account for 86% of bacteremia, 83% of meningitis, and 65% of otitis media in children younger than 6 years old (1987-1994)
  - Who?
  - When?
    - Dose 1: 2 months
      - May be given as early as 6 weeks
    - Dose 2: 4 months (at least 4 weeks after Dose 1)
    - Dose 3: 6 months (at least 4 weeks after Dose 2)
    - Dose 4: 12 – 15 months (at least 8 weeks after Dose 3)
    - If child is behind schedule, number of doses dependent on age
      - 7 – 11 months: 2 doses, one booster at 12 – 15 months
      - 12 – 23 months: 2 doses, at least 8 weeks apart
      - 24 – 59 months: one dose; consider two doses for children at high risk (i.e. sickle cell, asplenia, HIV, chronic illness, cochlear implant, immunocompromising conditions)

- Inactivated Polio vaccine
  - Who?
      - Booster shot if had completed initial series as child
      - If not previously immunized, need to complete initial series
  - When?
    - Dose 1:

- Dose 2:
- Dose 3:
- Dose 4: 4 – 6 years (do not need if Dose 3 given at age > 4 years)
- All doses should be separated by at least 4 weeks

- Measles, Mumps, Rubella (MMR)
  - Who?
    -
    -
  - When?
    - Dose 1: age 12 – 15 months
      - Does NOT count if given prior to 12 months
    - Dose 2: age 4 – 6 years
      - At least 4 weeks from Dose 1 if MMR
      - At least 3 months from Dose 1 if MMRV
    - Certain adults should receive two doses if not previously immunized
      -
      -
      -

- Varicella (Chicken pox)
  - Who?
    -
    - Any individual 13 years or older without evidence of immunity
      - Especially those at high risk for complications and healthcare personnel
  - When?
    - Dose 1:
    - Dose 2:
    - If exposed to individual with chicken pox, post exposure prophylaxis should be given within 3 to 5 days
  - What?
    - Two possible vaccines
      - Varicella (alone)
      - MMRV (in combination)
    -

- Hepatitis A
  - Who?
    -
    - Those older than 2 years old who fall into the following categories
      - Routine vaccination program available (areas with greater than 20 cases/ 100,ooo people)
      - Travel outside US, Western Europe, Australia, Canada, Japan
      - Chronic liver disease
      - Clotting factor disorder
      - MSM
      - IVDU
      - Experimental laboratory workers
      - Food handlers
  - When?
    - Dose 1:
    - Dose 2:

- *Neisseria meningitidis*; meningococcal vaccine
  - Who?
    -

-
    - Asplenia
    - Terminal complement deficiencies
    - HIV
    - Certain genetic factors
-
-
- Those traveling to endemic areas (e.g. sub-Saharan Africa "meningitis belt"
- Microbiologists working with *N. meningitidis*
- Military recruits

- When?
  - Dose 1:
- What?
  - Two different vaccines available with different age recommendations
    - Meningococcal Conjugate vaccine (MCV)
      - Preferred vaccine product
      - Conjugated vaccine product is believed to offer superior immune response
      - Currently recommended product for all individuals requiring immunization ages 2 – 55 years old
    - Meningococcal polysaccharide vaccine (MPSV)
      - Should be limited to persons > 55 years old
      - When MCV is not available

- Human Papillomavirus (HPV)
  - Who?
    -
    - Diagnosis of HPV does not exclude vaccination
  - When?
    - Dose 1: 11 – 12 years
    - Dose 2: 2 months after Dose 1 (may be shortened to 4 weeks)
    - Dose 3: 4 months after Dose 2 (may be shortened to 8 weeks)

- Varicella (Herpes Zoster)
  - Who?
    -

- ; pneumococcal polysaccharide vaccine (PPV)
  - Provides protection 23 strains of *S. pneumoniae* that account for 88% of bacteremic pneumococcal disease
  - Who?
    -
    -
    -

Chronic cardiac or pulmonary disease	Alcoholism	Diabetes
CSF leak	Alaska Natives	Certain American Indian populations
Asplenia	***Sickle cell***	***HIV***
Organ or bone marrow transplant recipient	***Leukemia***	***Lymphoma***
Multiple myeloma	***Nephrotic syndrome***	***Generalized malignancy***
Immunosuppressive chemotherapy	***Chronic renal failure***	***Cochlear implant candidate/ recipient***

  - When?
    - Children
      - Dose 1: 8 weeks after final dose of PCV
      - Dose 2: 3 – 5 years after initial PPV
        - Only for immunocompromised, sickle cell, asplenia
    - Adults
      - Dose 1:

- Dose 2:

- Special Vaccine Circumstances
  - Travelers
    - All travelers should be up-to-date with the recommended vaccinations
    - Additional vaccines may be recommended or required, depending on destination
      - Yellow fever
      - Typhoid
      - Japanese encephalitis
      - Rabies
    -
    - For additional information, consult the CDC travel website
      - http://wwwn.cdc.gov/travel/#
  - Health-Care Professionals
    - Recommended vaccines include

- Influenza
  - Background information
    - Viral infection typically seen in late fall and winter (November – May)
    - Two types of viruses capable of causing disease in humans
      - Influenza A (subtypes based on surface proteins)
      - Influenza B (two groups)
    - Two types of changes occur within influenza viruses
      - Antigenic drift :
        - Causes seasonal epidemics
      - Antigenic shift:
        - Causes pandemics
    - Transmission is primarily due to large droplets from respiratory tract of infected individuals but may also be transmitted by inaminate objects that come into contact with these droplets
    - Signs and symptoms usually abrupt and include
      - Fever
      - Myalgia
      - Sore throat
      - Nonproductive cough
      - Headahce
    - Typically resolves in 3 – 7 days in normally healthy individuals
    - More severe symptoms, including death, are seen more in the very young (<5 years), very old ($\geq$ 65 years old), and other that are generally not healthly
      - These individuals tend to compromise the majority of those patients who are hospitalized
      - Most people die from bacterial infections secondary to influenza, not the virus itself
  - Prevention Methods
    -
      - The MOST effective way for prevention
    -
      - Frequent hand washing
      - Improved respiratory hygiene
    -
  - Vaccination
    - Vaccines formulated every years based on prediction which strains will be the most prevalent
    - Always contain the same general formulation
      - Influenza A (H3N2)
      - Influenza B (H1N1)

- Influenza B
- Two types of flu vaccines
  - Live attenuated: FluMist®
  - Inactivated: Fluarix®, Fluvirin®, Fluzone®, FluLaval®, Alfuria®
- Differences between various flu vaccines
  - All contain same formulation
  - No real difference in efficacy between the live attenuated and inactivated formulations
  - Main difference is FDA approved ages
    - Fluzone: $\geq$ 6 months
    - Fluvirin: $\geq$ 4 years
    - Fluarix, FluLaval, Afluria: $\geq$ 18 years

    - FluMist: 2 -49 years
      - Contraindications/Precautions
        - Hypersensitivity to vaccine or eggs
        - Age < 2 years of >50 years
        - Persons with underlying medical conditions that are reasons to receive vaccination
        - Immunodeficiency
        - Children or adolescents on ASA therapy
        - History of Guillain-Barré syndrome
        - Pregnant women
        - History of asthma or recurrent wheezing in the past 12 months for children ages 2 – 4
        - Consider vaccinating another time if significant nasal congestion
        - Household contacts of severely immunosuppressed could theoretically shed virus after vaccination and should be vaccinated with inactivated vaccine
-

- Who should be vaccinated?
  -

    - Target specifically children 6 months – 4 years in vaccine shortage
  -

  - Children and adolescents on ASA therapy
  -

  - Individuals with
    - COPD
    - Cardiovascular disorders (excluding HTN)
    - Renal disorders
    - Hepatic disorders
    - Hematological disorders
    - Diabetes (or other metabolic disorders)
    - Immunosuppression
    - Conditions that may compromise respiratory function (e.g. seizures, cognitive dysfunction, spinal cord injuries)
  - Nursing home and long-term care facility residents
  -

  -

- Antivirals
  - Two classes of antiviral agents used to treat influenza
    - Neuraminidase inhibitors (oseltamivir (Tamiflu®), zanamivir (Relezna®))
      - MOA:

    - Adamantanes (amantadine (Symmetrel®), rimantidine (Flumadine®)
      - MOA:

      -

- Use of antivirals
  - Prophylaxis
    - Consider using
      -
      -
      -
  - Treatment
    - Outpatients
      - Must be started with hours of treatment onset
      - Will reduce illness about 1.5 days
    - Inpatients
      - Oseltamivir may be associated with a mortality reduction in patients hospitalized with influenza
      - Likely underused in this setting
  - Dosing and Adverse Effects

Drug	Adult Dose	Pediatric Dose	Side Effects	Dose adjustment?
Oseltamivir	**Tx**: 75 mg BID x 5 days **Px**: 75 mg qday > 7 days	<15 kg: 30 mg BID 15 – 23 kg: 45 mg BID 23 – 40 kg: 60 mg BID > 40 kg: 75 mg BID Duration: 5 days	N/V Bronchitis Insomnia Vertigo *Neuropsychiatric events* (rare)	Renal CrCL 10 – 30 mL/min: 75 mg qday
Zanamivir	10 mg (2 inhalations) BID x 5 days	Age ≥ 7 years: 10 mg (2 inhalations) BID x 5 days	Sinusitis Dizziness Fever/chills Bronchospasm (rare)	None

- Resources
  - The Pink Book (Epidemiology and Prevention of Vaccine-Preventable Diseases)
    - Updated yearly
    - Available at http://www.cdc.gov/vaccines/pubs/pinkbook/default.htm
  - The Yellow Book (CDC Health Information for International Travel0
    - Updated every two years
    - Available at http://wwwn.cdc.gov/travel/contentYellowBook.aspx
  - Prevention and Control of Influenza – Recommendations of Advisory Committee on Immunization Practices (ACIP), 2008. MMWR 2008 Jul 17; Early Release: 1 – 60
    - Available at http://www.cdc.gov/mmwr/preview/mmwrhtml/rr57e717a1.htm